

extending the period for response up to and including June 9, 2002. The Commissioner is hereby authorized to charge the appropriate small entity fee for this three-month extension, and to charge any other fees which may be due in connection with the filing of this response to Kenyon & Kenyon's Deposit Account No. 11-0600.

REMARKS

The Examiner stated that restriction to one of the following ninety-eight (98) inventions, which the Examiner has broken down into five (5) sets of groups, is required under 35 U.S.C. § 121:

Groups 1-48 Claims 1-9, 57, 58, 88-95, 96-99, 145, 146, 148, drawn to isolated nucleic acids of SeqIDNos: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93 or 94, respectively for Groups 1-48, encoding the genes namely, calA, calB, calC, calD, calE, calF, calG, calH, calI, calJ, calK, calL, calM, calN, calO, calP, calQ, calR, calS, calT, calU, calV, calW, calX, 6MSAS, ActI, ActII, ActIII, orf1, orf2, orf3, orf4, orf5, orf6, orf7, orf8, orf1, orfII, orfIII, orfIV, orfV, orfVI, orfVII, orfVIII, orfIX, orfX, orfXI, an IS-element gene respectively for Groups 1-48, and to a nucleic acid sequence encoding the protein of SeqIDNos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 or 95, respectively for Groups 1-47, vector and host cell, classified in class 435, subclass 320.1.

Group 49: Claim 100, drawn to a method of purifying calicheamicin using affinity

chromatography, classified in class 435, subclass 803.

Groups 50-96: Claims 101, 149, drawn to a polypeptide of SeqIDNos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92 or 95, respectively for Groups 50-96, classified in class 530, subclass 300.

Group 97: Claim 142, drawn to a method of conferring calicheamicin resistance in a subject by ex vivo methods, classified in class 424, subclass 93.21.

Group 98: Claim 143, 144, drawn to a compound, classified in class 260.

Applicant respectfully **traverses** this restriction requirement on several grounds.

Nonetheless, applicant wishes to elect to pursue with traverse the invention of Groups 1-48 with respect to the gene calS defined by SEQIDNo. 35, and also the nucleic acid defining the protein of SEQIDNo. 36, a vector comprising that nucleic acid and a host cell expressing a protein encoded by that nucleic acid. Claims readable on this invention include claims 1-9, 57, 88-95, 96-99, 145-146, and 148.

The grounds for traversal are as follows:

Groups 1-48 corresponding to claims 1-9, 57, 58, 88-99, 145-146, and 148 provide forty-eight genes, twenty-seven of which encode structural genes within the calicheamicin-biosynthetic gene cluster with the remainder of the genes encoding functions in the calicheamicin biosynthetic pathway.

Specifically claimed in Groups 1-48 are the nucleic acids encoding these genes (Claims 1-9, 57-58, and 148), the proteins encoded by the nucleic acids claimed (claims 145-146), and vectors and host cells containing the same (claims 88-96).

Applicant submits that restriction to examination of a single gene within this group of forty-eight (48) is improper under MPEP § 803.04.

MPEP § 803.04 states the following:

..... to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden in the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR 1.141 *et seq.* and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See *Examination of Patent Applications Containing Nucleotide Sequences*, 1192 O.G 68 (November 19, 1996).

Section 803.04 further states that:

It has been determined that *normally* ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein not considered to be independent and distinct inventions and will continue to be examined together. (*emphasis added*)

Applicant respectfully requests that the Examiner limit the restriction to a five-way restriction as defined by the groups identified by the Examiner as (1) Groups 1-48 (claims 1-9, 57, 58, 88-95, 96-99, 145, 146 and 148), (2) Group 49 (claim 100), (3) Groups 50-96 (claims 101 and 149), (4) Group 97 (claim 142) and (5) Group 98 (claims 143 and 144).

As the MPEP states, while *normally* ten specifically selected sequences constitute a reasonable number for examination purposes, “in addition to those specifically selected sequences, those sequences which are patentably indistinct from those selected sequences will also be examined.” MPEP § 803.04. All forty-eight (48) identified and claimed genes encode for proteins and enzymes used in the calicheamicin biosynthetic pathway and construction of calicheamicin’s distinct aryltetrasaccharide structural region and the aglycone (warhead) region. Twenty-seven of the forty-eight genes encode structural proteins which define the aryltetrasaccharide and aglycone moieties of the potent antibiotic and anti-tumor agent, calicheamicin. (*see* pages 22-23 of the specification).

Since all forty-eight (48) genes identified and sequenced are part of the "calicheamicin gene cluster," applicant asserts that it would not be unduly burdensome for the Examiner to search the databases regarding these sequences. It would, however, be a tremendous financial burden for applicant to have to file 98 separate applications covering this invention.

Applicant, Memorial Sloan-Kettering Cancer Center, the organization to which this patent application will be assigned, is a non-profit organization seeking to pursue successful cancer therapies. Calicheamicin is a potent anti-tumor agent and the elucidation of the calicheamicin biosynthetic gene cluster is a great advance toward the future development of new and clinically useful therapeutic agents.

If, however, the Examiner believes that such invention should be further restricted than as proposed above, applicant respectfully proposes the following restriction for the claims defined by Groups 1-48 (Claims 1-9, 57, 58, 88-99, 145-146, and 148):

Section 803.04 of the MPEP states that *normally* ten (10) sequences constitute a reasonable number for examination; however, instead of simply randomly dividing the forty-eight (48) separate sequences into groups of four sets of 10 sequences and one set of eight sequences, applicant proposes that the forty-eight nucleic acid sequences be more logically divided into four separate applications. This proposed "logical" division would also aid the Examiner by reducing her burden in searching. Specifically, applicant proposes that the specifically-identified sequences be grouped based on their function as identified by BLAST analysis and as described on pages 22-23 and 27-28 of the specification. Specifically, proposed groups of sequences (restricted out into separate applications) would be as follows:

- 15 genes that encode for the aryltetrasaccharide moiety (calD, CalE, calF, calG, calH, calJ, calK, calN, calO, calQ, calS, calT, calV, calX, and 6MSAS);
- 12 genes which encode for the aglycone moiety (calP, calS, calV, calW, ActI, ActII, ActIII, orfI, orfIII, orfV, orfVI, orfVII);

- 13 genes involved in membrane transport, regulation, DNA movement and/or resistance (calA, calB, calC, calI, calM, calR, orf4, orf8, orfVIII, orfIX, orfX, orfXI, IS-element); and
- the remaining 8 genes which, at present, have unknown function (orf7, orf2, orf3, orf5, orf6, orf7, orfII and orfIV).

Thus, the portion of claims 1-9, 57-58, 88-99, 145-146, and 148 encoding calD, CalE, calF, calG, calH, calJ, calK, calN, calO, calQ, calS, calT, calV, calX, and 6MSAS; the nucleic acid sequences encoding those genes (SEQIDNos. 11, 94, 13, 5, 4, 17, 19, 25, 27, 31, 35, 37, 41, 45, 43, and 47, respectively); the nucleic acid sequences encoding the proteins defined by these sequences, and the vectors and host cells incorporating these genes would be examined together.

Similarly, the portion of claims 1-9, 57, 58, 88-95, 96-99, 145-146, and 148 encoding the 12 genes which encode for the aglycone portion of calicheamicin as well as the portion of corresponding claims to nucleic acids, nucleic acid sequences encoding the proteins, and vectors and host cells comprising the same would be examined together.

Similarly, the portion of claims 1-9, 57, 58, 88-95, 96-99, 145-146, and 148 which encode the 13 genes involved in membrane transport, regulation, DNA movement and/or resistance would be examined together as well as the portion of corresponding claims to nucleic acids, nucleic acid sequences encoding the proteins, and vectors and host cells comprising the same would be examined together.

In addition the portion of claims 1-9, 57, 58, 88-95, 96-99, 145-146, and 148 which encode the 8 remaining genes of unknown function, their nucleic acid sequences, and vectors and host cells comprising the same would be examined together.

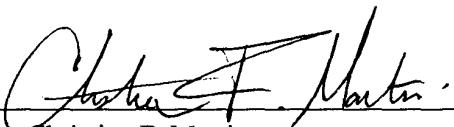
The undersigned agent for Applicant would like to thank the Examiner for considering this draft response to the Restriction Requirement and, in advance, for the time to be expended in the upcoming telephone conference.

Respectfully submitted,

KENYON & KENYON

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